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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,608	12/12/2003	Marcel P. Bruchez	5100-0702.20	1956
20855	7590	12/29/2005	EXAMINER	
ROBINS & PASTERNAK 1731 EMBARCADERO ROAD SUITE 230 PALO ALTO, CA 94303			DO, PENSEE T	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,608	BRUCHEZ ET AL.	
	Examiner Pensee T. Do	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 29 September 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1 and 3-41 is/are pending in the application.
- 4a) Of the above claim(s) 17-37 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,3-16 and 38-41 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) 17-37 are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____.

DETAILED ACTION

Amendment Entry & Claim Status

The amendment filed on September 29, 2005 has been acknowledged and entered.

Claims 1, 3-41 are pending.

Claims 1, 3-16, 38-41 are being examined.

Claims 17-37 are withdrawn from further consideration according to Ochiai Guidelines.

Withdrawn Rejection(s)

Rejection under 112, 2nd paragraph is withdrawn herein.

Maintained Rejection(s)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-7, 10-13, 16, 38, 39, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bawendi et al. (US 6,306,610) in view of Rothbard et al. (US 6,306,993).

Bawendi teaches a composition comprising fluorescent semiconductor nanocrystals associated to a molecule such as cells, prokaryotic or eukaryotic. The semiconductor nanocrystals comprise a CdSe core and a ZnS shell. The composition is

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also associated with cell membranes. (see col. 3, line 60-col. 4, line 62; col. 19, lines 58-60; col. 20, lines 51-59; col. 29, lines 41-42).

However, Bawendi fails to teach the nanoparticle is associated with a cationic polymer capable of enhancing the transport of the semiconductor nanoparticle across a biological membrane; wherein the cationic polymer has from 5 to 25 contiguous Lys and/or Arg residues. Bawendi also fails to teach a kit comprising a semiconductor nanoparticle complex according to claims 1, 12, 16 and instructions for preparing the encoded cells using the semiconductor nanoparticle complex. Bawendi also fails to teach the cationic polymer is a tat peptide from protein transduction domain of the HIV tat protein.

Rothbard teaches methods and composition for transporting drugs and macromolecules across biological membranes wherein the biological membranes are contacted with a conjugate containing a biologically active agent that is covalently attached to a transport polymer. Such transport polymer has 6 to 25 subunits of L-Arginine. The transport enhancing polymers are exemplified by peptides in which arginine residues constitute the subunits. Exemplary eukaryotic cell membranes of interest include membranes of dendritic cells, epithelial cells, endothelial cells, keratinocytes, muscle cells, fungal cells, bacterial cells, plant cells and the like. Biological active agents are macromolecules such as nucleic acids, peptides, proteins and analogs thereof. The agent may be linked to the polymer by a linking moiety. The composition includes a conjugate containing a biological active agent covalently attached to at least one transport polymer and can be packaged with instructions for

using it. (see col. 2, line 44-col. 4, line 45; col. 5, lines 47-58). The transport polymers contain short-length polymers from 6 to 25 subunits. The conjugate is effective to enhance the transport rate of the conjugate across the biological membrane relative to the transport rate of the non-conjugate biological agent alone. (see col. 6, line 63-col. 7, line 5). Detecting uptake of macromolecules may be facilitated by attaching a fluorescent tag. (see col. 11, lines 3-4). Fluorescently labeled peptide polymers composed of 6 or more arginine residues entered cells more efficiently than the tat sequence 49-57 in fig. 1 (see col. 11, lines 30-40). Since the polymer of Rothbard composes of 6 to 25 contiguous Arg residues, it must be a cationic polymer.

Since Bawendi and Rothbard both teach using a label such as nanocrystals for cells or cell membrane, it would have been obvious to one of ordinary skills in the art to associate the polymer, which comprises of 6 to 25 subunits of Arg residue, taught by Rothbard to the nanocrystals as a fluorescent label and use in the composition of Bawendi because macromolecules such as peptides and oligonucleotides experience difficulty in passing across the biological membrane and having a polymer as that of Rothbard enhances trans-membrane transport. Furthermore, the nanocrystals of Bawendi can be used a label which associates with the polymer to so that measures of biological molecules transported across the biological membrane can be easily detected because the nanocrystals of Bawendi associates with the biological membrane. Regarding claims 38, 39 and 41, it would have been obvious to one of ordinary skills in the art to package the combined composition taught by Bawendi and Rothbard with

instruction for using it for economical convenience since Rothbard teaches packaging the polymer with biological active agent into a kit with instructions for using it.

Claims 8, 9, 14, 15 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bawendi et al. (US 6,306,610) in view of Frankel et al. (US 5,652,152).

Bawendi has been discussed above.

However, Bawendi fails to teach that the cationic polymer is tat peptide from the protein transduction domain of the HIV tat protein and a kit comprising the composition of claim 14 with instruction of using. Bawendi also fails to teach the sequence ID NO. 1 comprising of Arg Lys Lys Arg Arg Gln Arg Arg Arg.

Frankel teaches intracellular delivery of cargo molecules by the use of transport polypeptides which comprise HIV tat protein or one or more portions thereof and which are covalently attached to the cargo molecules. The transport polypeptides are characterized by the presence of the tat basic region (amino acids 49-57). The biological active cargo molecules such as polypeptides, nucleic acids are delivered/transported into the cytoplasm and nuclei of cells in vitro and in vivo. (see abstract). Label such as a fluorescent was used to study the transported molecules across the cell membrane. The label is attached to the tat peptide. (see col. 42, lines 24-29). Frankel teaches sequence ID No. 4, amino acids 12-20, comprising Arg Lys Lys Arg Arg Gln Arg Arg Arg. (see col. 55-56, sequence ID. NO. 4).

It would have been obvious to one of ordinary skills in the art to use the HIV tat peptide for transporting biological molecules across the cell membrane as taught by

Frankel and attach it to a fluorescence semiconductor nanocrystal which associates to a cell membrane so that when biological molecules to be transported reach the cell membrane, they can be transported effectively and efficiently with the aid of the tat peptide and their activity or measurement can be detected by the nanocrystals since the nanocrystals have a spectral emission that is tunable to a desired wavelength, and wherein said wavelength provides information about a biological state or event. It would have been obvious to one of ordinary skills in the art to package the combined composition into a kit with instruction of using it for economic convenience since Frankel teaches that the tat polypeptide can be used as research laboratory reagents, either alone or as part of a transport polypeptide conjugation kit. (see col. 7, lines 30-32).

Response to Arguments

Applicant's arguments filed September 29, 2005 have been fully considered but they are not persuasive.

Applicants argue that because Bawendi fails to teach certain limitations of the claims, Bawendi therefore fails to provide any motivation for such a complex of the nanocrystal bound to the cationic polymer. Applicants further argue that Rothbard pertains to the transport of drugs and macromolecules across biological membranes but not nanocrystal. Rothbard is not attempting to enhance transport of a label, let alone a semiconductor nanocrystal, across a biological membrane. Applicants further submit that the semiconductor nanocrystals are considered to be a physical form somewhere between molecular and bulk phase materials. There is absolutely no reason to believe that the carrier peptides employed to transport organic molecules across biological

membranes would also successfully transport inorganic nanocrystals across biological membrane. Moreover, semiconductor nanocrystals comprising a shell and a core, are complex multilayer structures that have an average composition, analogous to a polymer. These complex structures are not the same as the molecules transported by Rothbard and there is no suggestion in Rothbard to use a transport polymer with such structure. Regarding the 103 rejection by Bawendi in view of Frankel, Applicants again argue that Frankel, like Rothbard, does not supply the missing links. Frankel pertains to the delivery of nucleic acid and protein molecules, not crystalline particles, as claimed.

Rothbard and Bawendi teach using labels such as fluorescent labels to detect activity within a cell. Bawendi teaches that the fluorescent semiconductor nanocrystals can be used to visualize location in a cell. (see col. 22, lines 30-34). Rothbard teaches that the fluorescently labeled peptide polymers or the transport peptide linked polymer is used to assess cellular uptake of biological molecules being transported across the cell membrane. (see col. 11, lines 3-33). Frankel also teaches using fluorescent label to study the transported molecules. The label is attached to the tat peptide. (see col. 42, lines 24-29). Thus, one of ordinary skills in the art would have been motivated to combine these references based on those teachings above of Bawendi and Rothbard, or Bawendi and Frankel. Fluorescent tags can be used to assess the cellular uptake of biomolecules and nanocrystals in Bawendi is a fluorescent label. Thus, one of ordinary skills in the art would have reasonable expectation of success when linking the fluorescent nanocrystal of Bawendi to a transport peptide of Rothbard or Frankel. Applicants argue that "There is absolutely no reason to believe that the carrier peptides

employed to transport organic molecules across biological membranes would also successfully transport inorganic nanocrystals across biological membrane". Rothbard and Frankel teach the same transport polymer as the claimed invention, and that such polymer can be linked to a fluorescent tag. Bawendi teaches the same fluorescent semiconductor nanocrystal as the claimed invention and it is a fluorescent tag. Thus, one of ordinary skills in the art would have success in combining these references. If Applicants argue that the transport polymer of Rothbard and Frankel cannot transport inorganic nanocrystal across a biological membrane, then it is no difference that Applicants are admitting that the present invention is not enable.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
December 22, 2005


LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

12/27/05